PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/002865	01.07.2004	01.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K39/118, A61K39/09, A61K39/02, A61K39/295, G01N33/569, A61P31/04, A61P31/12, C07K16/12

Applicant
THE ROYAL VETERINARY COLLEGE

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material:

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material:

☒ in written format

☒ in computer readable form

c. time of filing/furnishing:

☐ contained in the international application as filed

☐ filed together with the international application in computer readable form

☒ furnished subsequently to this Authority for the purposes of search

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☐ The following document has not been furnished:

   ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 16-19,29,32-34,43-48,51 (with respect to IA)

because:

☒ the said international application, or the said claims Nos. 16-19,29,32-34,43-48,51 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	9-22,25,26,30,32-37,45-48,51
	No:	Claims	1,2,8,23,24,27,29,31,52,54
Inventive step (IS)	Yes:	Claims	43,44,53
	No:	Claims	1-42,45-52,54
Industrial applicability (IA)	Yes:	Claims	1-15,20-28,30,31,35-42,49,50,52-54
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and/or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Reference is made to the following documents:

D1: US-A-5 583 014

D2: EP-A-1 023 903

D3: WIDDERS P R ET AL: "Immunisation of mares to control endometritis caused by Streptococcus zooepidemicus" RESEARCH IN VETERINARY SCIENCE, vol. 58, no. 1, 1995, pages 75-81

D4: EP-A-0 415 794

D5: HECHARD CELINE ET AL: "Protection evaluation against Chlamydophila abortus challenge by DNA vaccination with a dnaK-encoding plasmid in pregnant and non-pregnant mice" VETERINARY RESEARCH (PARIS), vol. 33, no. 3, May 2002 (2002-05), pages 313-326

D6: "Nobivac Forcat" VETERINARIA NEWS, [Online] 2002, pages 1-6,

D7: DATABASE PHIN STN, 10 May 2002 (2002-05-10), "Nobivac Forcat in Switzerland"

D8: US 2003/021801)

D9: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; March 2001 (2001-03), OBUKHOV I L ET AL: "Development of vaccine against chlamydiosis in cats, dogs and fur-bearing animals" Database accession no. PREV200100271011

D10: WO 86/02355

D11: WO 87/00531

D12: WOLOSZYN S ET AL: "Infectious tracheobronchitis in dogs." MEDYCYNA WETERYNARYJNA, vol. 50, no. 9, 1994, pages 428-431

D13: CHALKER VICTORIA J ET AL: "The association of Streptococcus equi subsp. zooepidemicus with canine infectious respiratory disease." VETERINARY MICROBIOLOGY, vol. 95, no. 1-2, 29 August 2003 (2003-08-29), pages 149-156

D14: WO 2004/011651

Re item III:

Claims 16-19 and 32-34 relate to methods of treatment of the human or animal body by therapy. The wording of claims 29, 43-48 and 51 is such that it embraces a

method of treatment of the human or animal body by therapy. Thus claims 16-19, 29, 32-34, 43-48 and 51 relate to subject-matter considered by this Authority to be covered by the provisions of R. 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

Re item V:

1.1 D1 discloses a vaccine comprising enzyme-detergent extracted S. zooepidemicus (c. 1, l. 50-51; c. 5, l. 15-24; Example 1; claim 1).
D2 teaches a vaccine comprising life attenuated S. zooepidemicus (c. 4, l. 14-16; Example 2; claims 1, 3-5).
D3 discloses a vaccine comprising an antigenic extract of S. zooepidemicus (p. 75, c. 1, para. 2 - p. 76, c. 1, para. 4).
D4 teaches a vaccine comprising either Chlamydia psittaci or M. cynos (p.2. l. 1 - p. 3, l. 19; Example 10; claims 1 and 2).
D5 teaches a vaccine against Chlamydophila abortus comprising its dnaK gene (abstract; p. 316, c. 1, para. 2 - c. 2, para.3).
D6 (whole document) and D7 (whole document) teach a vaccine comprising life attenuated Chlamydophila felis (Nobivac Forcat).
D8 discloses vaccines against C. trachomatis, C. psittaci and C. pneumoniae comprising the respective PorB polypeptides (claims 1-18).
D9 teaches a vaccine against Chlamydiosis in dogs comprising inactivated Chlamydia (whole document).
As there are no specific features suggested that are required to achieve an immunogenicity in dogs, the vaccines disclosed in D1-D9 are considered to destroy the novelty of claim 1 (Art. 33(2) PCT).

1.2 In D1-D9 (supra) the vaccines are used in medicine. Hence, claim 23 lacks novelty over any of D1-D9 (Art. 33(2) PCT).

1.3 D6 also discloses a kit comprising the Nobivac Forcat vaccine (c. 4, para. 3). The subject-matter of claim 27, thus, lacks novelty over D6 (Art. 33(2) PCT).
D8 teaches a kit comprising the PorB polypeptide (c. 14, para. 3), thereby destroying

the novelty of claim 27 (Art. 33(2) PCT).
D11 teaches a kit comprising an antigen of S. zooepidemicus. As any antigen of S. zooepidemicus is considered to be capable of raising an immune response in dogs (p. 15, l. 13 - p. 16, l. 5), the subject-matter of claim 27 lacks novelty over D11 (Art. 33(2) PCT).
Moreover, as the only feature of the kit according to claim 27 is the agent capable of raising an immune response against any one of the microorganisms listed, and as each of D1-D5, D7 and D9 discloses such an agent (cf. V.1.1), the subject-matter of claim 27 also lacks novelty over any of said documents (Art. 33(2) PCT).

1.4 D4 discloses a method of generating a monoclonal antibody directed at S. zooepidemicus as well as such an antibody (p. 15, l. 13 - p. 16, l. 5; Example 1; claim 9).
D8 teaches anti-PorB antibodies as well as a method of generating the said (c. 10, para. 3-5; c. 19, para. 4).
D10 teaches monoclonal antibodies to C. trachomatis and C. psittaci as well as a method of generating the said antibody by hybridoma technology(examples 1-3; claims 1-8).
D11 teaches a monoclonal antibody specific for S. zooepidemicus as well as a method of generating the said antibody by hybridoma technology (Example 1; claim 9).
Hence, the subject-matter of claims 29 and 31 is anticipated by D4, D8, D10 and D11 (Art. 33(2) PCT).

1.5 D3 discloses an ELISA for the detection of antibodies generated against S. zooepidemicus upon vaccination of mares with a bacterial preparation of S. zooepidemicus. In said ELISA the said preparation is coated onto microtiter plates and bound antibodies are detected by a sandwich assay involving a detectable label conjugate which binds to antibodies bound to the microtiter plate (p. 76, c. 2, last para.).
D5 teaches an ELISA for the detection of DnaK-directed antibodies, wherein DnaK is immobilised to a support and peroxidase-conjugated anti-mouse antibodies are used to detect the binding of antibodies contained in the sample to the immobilised DnaK (p. 317, c. 1, para. 2).

D8 teaches a sandwich immunosorbent assay for the detection of PorB-directed antibodies wherein PorB is immobilised to a solid support and labelled secondary antibodies are used to detect antibodies bound to the immobilised PorB (c. 11, para. 3 - c. 14, para. 1).
The disclosures of D3, D5 and D8 are thus prejudicial to the novelty of claims 52 and 54 (Art. 33(2) PCT).

1.6 D1-D3 (supra) disclose the additional feature suggested by claim 2 and 24.
Moreover, the additional features according to claim 8 are also disclosed in D1 (supra) and D3 (supra).
D4 (supra) teaches the additional features suggested by claims 3, 5, 8 and 24.
D5 (supra) discloses the additional features suggested by claims 4 and 24.
The additional features according to claims 5, 6 and 24 are disclosed in D6 (supra) and D7 (supra).
D8 (supra) teaches the additional features suggested by claims 5 and 7.
D9 (supra) discloses the additional features proposed by claims 24 and 25.
Thus, claims 2-8, 24 and 25 do not establish novelty over the prior art (Art. 33(2) PCT).

1.7 The subject-matter of claims 9-22, 26, 28, 30, 32-51 and 53 is novel as the prior art does not disclose the combination of features suggested by any of these claims 8 (Art. 33(2) PCT).

2.1 The description only teaches an association of S. zooepidemicus, M. cynos and positive Chlamydophila PCR with CIRD. No support is provided for any prophylactic/therapeutic effect of a vaccine comprising an agent capable of raising an immune response against any of these organisms in dogs which would be the basis for acknowledging the problem of vaccinating a dog against CIRD or of treating CIRD in a dog using said vaccine as being solved. Hence, the subject-matter of claims 16 and 17 is not considered to involve an inventive step (Art. 33(3) PCT).

2.2 For similar considerations (cf. V 2.1) also the subject-matter of claims 20, 21, 32, 33, 35, 36 and 40 is not considered to involve an inventive step (Art. 33(3) PCT).

2.3 The combination of antibodies suggested by claim 38 is a mere juxtaposition of known antibodies (cf. V 1.4) which do not have any non-obvious inter-relation ship and whose inclusion into a single composition, thus, does not establish an inventive step (Art. 33(3) PCT).

2.4 For these considerations (cf. V 2.3) also dependent claim 39 is not considered inventive (Art. 33(3) PCT).

2.5 D12 teaches an association of CIRD with M. cynos (p. 428, c. 1, para. 1; p. 429, c. 1, para. 1). Based on this teaching and in applying routine experimentation the skilled person would devise a method of determining whether a dog has CIRD by identifying the said microorganism in a sample from the dog. Thus, claim 45 is not considered to involve an inventive step (Art. 33(3) PCT).

2.6 The subject-matter of claim 18 differs from e.g. D3 in that an immune response is stimulated in dogs and not in mares. There is no support for said stimulation to have a technical effect, namely of preventing, curing or alleviating CIRD in dogs (cf. V 2.1). Therefore, the selection of dogs for immunisation is considered arbitrary and does not establish an inventive step (Art. 33(3) PCT).

2.7 As there is also no support for an agent according to claim 9 to induce an immune response protective against or curative for CIRD, the same considerations as under V 2.1 lead to the conclusion that this claim does not involve an inventive step (Art. 33(3) PCT).

2.8 For the considerations formulated under V 2.1, 2.2 and 2.7, also the subject-matter of claims 10-15, 22, 26, 34, 41 and 42 is not considered inventive (Art. 33(3) PCT).

2.9 The method of claim 30 is a routine modification of the methods of generating an antigen-specific mAb as suggested by any of D4, D10 and D11 (cf. V 1.4) which does not result in any unforeseeable technical effect, and which, thus, does not establish an inventive step (Art. 33(3) PCT).

2.10 In view of the arguments given under V 2.1, 2.6 and 2.7 the kit according claim 28

relates to an arbitrary juxtaposition of components which do not show any non-obvious inter-relationship. Hence, said claim does not involve an inventive step (Art. 33(3) PCT).

2.11 The additional features suggested by claims 46, 47, 49 and 51 are a matter of routine experimentation and do not produce any unforeseeable technical effect and, therefore, do not establish an inventive step (Art. 33(3) PCT).

2.12 The additional features suggested by claims 48 and 50 have no limiting effect with respect to the alternative in the antecedent relating to M. cynos and thus do not establish an inventive step over D12 (cf. V 2.5 and 2.11)(Art. 33(3) PCT).

2.13 The subject-matter of claim 43 solves the problem of determining whether a dog has been exposed to CIRD-associated Chlamydophila. The solution involves identifying in a sample from the dog a CIRD-associated Chlamydophila species or an antibody thereto. This method is based on the observed association of CIRD with certain Chlamydophila species which is not suggested by the prior art. Hence, the subject-matter of claim 43 involves an inventive step (Art. 33(3) PCT).

2.14 Claim 53 suggest an immunosorbent assay comprising a solid phase comprising antigens of at least two of S. zooepidemicus, M. cynos and Chlamydophila associated with CIRD. This solid phase solves the technical problem of increasing the sensitivity of detecting antibodies associated with CIRD. D12 teaches only the association of M. cynos with CIRD. The skilled person would not have an incentive to immobilise any of the other two antigens. Claim 53 is, therefore, considered to involve an inventive step (Art. 33(3) PCT).

2.15 The considerations of V 2.13 also apply to dependent claim 44 (Art. 33(3) PCT).

3.1 For the assessment of the present claims 16-19, 29, 32-34, 43-48 and 51 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may

allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

3.2 The subject-matter of claims 1-15, 20-28, 30, 31, 35-42, 49, 50 and 52-54 is considered to be industrially applicable (Art. 33(4) EPC).

4.1 Claims 1-7, 9-15, 18-23, 26-28, 40-42 and 52 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved ("agent capable of raising an immune response against ..."), which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result. It cannot be determined which compounds fall under the said functional definition.

4.2 Also in claim 43 the subject-matter is considered to be defined in terms of a result to be achieved ("a Chlamydophila species associated with CIRD"), thereby creating unclarity (Art. 6 PCT).

4.3 Whereas, the introductory part of claim 52 appears to relate to a method, the technical features proposed refer to a device. This inconsistency renders the category of said claim unclear (Art. 6 PCT)

Re item VI:

Should the priority of the present application not be valid, the D13 and D14 would be relevant with respect to novelty and inventive step (Art. 33(2) and (3) PCT).